07 621092

(GI 5181)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	Group Art Unit:
R. Kaufman et al	Examiner:
Serial No.	
Filed: Herewith	
For: METHOD OF INCREASING YIELD OF MATURE PROTEINS IN MAMMALIAN CELLS	

Hon. Commissioner of Patents and Trademarks,
Washington, DC 20231

INFORMATION DISCLOSURE STATEMENT

Sir:

The following documents are submitted to the Examiner, pursuant to 37 CFR sections 1.56 and 1.97. Form PTO-1449 is attached and copies of the references having publication dates prior to the priority date of this application are enclosed herewith.

Other Documents

(AR) D. C. Foster et al, Thrombosis and Haemostasis, 62:321 (1989)

(AS) Claudia K. Derian et al, J. Biol. Chem., 264(12):6615-6618 (1989)

(AT) Randal J. Kaufman et al, J. Biol. Chem., 261(21):9622-9628 (1986)

(AU) Ans M. W. van den Ouweland et al, Nucl. Acids. Res., 18(3):664 (1990)

(AV) Steven P. Smeekens et al, J. Biol. Chem., 265(6):2997-3000 (1990)

(AW) Bruce Furie et al, Cell, 53:505-518 (1988)

(AX) Gary Thomas et al, Science, 241:226-230 (1988)

(AY) Dickerson et al, J. Biol. Chem., 265:2462 (1990)

(AZ) Achstetter et al, EMBO J., 4:173 (1985)

(AAR) Mizuno et al, Biochem. Biophys. Res. Commun., 144:807 (1987)

(AAS) Julius et al, Cell, 37:1075 (1984) [Julius I]

(AAT) Julius et al, Cell, 36:309 (1984) [Julius II]

(AAU) Roebroek et al, EMBO J., 5:2197 (1986)

(AAV) Wang et al, Proc. Natl. Acad. Sci. USA, 87:2220-2224 (1990)

REMARKS

D. C. Foster et al (AR) teach that human protein C can be readily synthesized and secreted in several mammalian cell lines. However, cell lines vary considerably in their ability to remove the dibasic pair in the protein C precursor and secrete a mixed population of one-chain and two-chain forms of the protein.

Claudia K. Derian et al (AS) refer to the identification of the gamma-carboxyglutamate (GLA) domain of Factor IX as a major cell binding domain.

Randal J. Kaufman et al (AT) refer to the first purification and characterization of a biologically active, gamma carboxylated vitamin K dependent protein expressed in a recombinant DNA system, the protein being Factor IX.

van den Ouweland et al (AU) present the complete nucleotide sequence of the fur coding sequence. The structural homology between the human fur gene product and the subtilisin-type serine protease encoded by the KEX2 gene of the yeast Saccharomyces cerevisiae is compared.

Steven P. Smeekens et al (AV) refer to the identification of human insulinoma cDNA that encodes a protein homologous to the precursor processing KEX2 endoprotease of yeast by using PCR technique.

Bruce Furie et al (AW) show the sequences of the propeptide domains of vitamin K-dependent blood coagulation proteins. The size of the propeptide has been established for Factor IX and protein C.

Gary Thomas et al (AX) refer to the expression of KEX2 enzyme activity in mammalian cells. Specifically, it was found that yeast KEX2 endopeptidase correctly cleaves a neuroendocrine prohormone in mammalian cells.

Dickerson et al (AY) refer to the site-specific endoprotease cleavage activity of prohormones.

Achstetter et al (AZ) refer to the identification of proteinase yscF and carboxypeptidase yscα which are involved with propheromone processing in the yeast S. cerevisiae.

Mizuno et al (AAR) refer to the partial purification of a novel endoprotease which cleaves on the carboxyl side of paired basic residues in S. cerevisiae.

Julius et al (AAS) refer to the isolation of KEX2 as the structural gene for Lys-Arg-cleaving endopeptidase. This endopeptidase is required for the processing of yeast prepro-α-factor.

Julius et al (AAT) refer to the proteolytic processing of a prepro-α-factor in the S. cerevisiae secretory pathway.

Roebroek et al (AAU) refer to the characterization of fur as encoding a protein with receptor-like features and some features of its putative translation product, furin.

Wang et al (AAV) refer to the purification and characterization of a recombinant human bone morphogenetic protein (BMP-2A) which has potential as a therepeutic for promoting de novo bone formation in humans.

No representation is made hereby that these documents provide all of the art and the Examiner is presumed to conduct an independent search of the art. However, these documents do form all of the relevant art of which applicants are presently aware. Should applicants become aware of additional relevant art during the prosecution of this application, applicants will bring such art to the attention of the Examiner by means of a supplemental Information Disclosure Statement.

The Examiner is respectfully requested to consider the enclosed documents during the course of the examination of this application.

Respectfully submitted,

HOWSON AND HOWSON
Attorneys for Applicant

By Mary E. Bak
Mary E. Bak
Registration No. 31,215
Spring House Corporate Center
Box 457
Spring House, PA 19477
(215) 540-9200

CERTIFICATE UNDER 37 CFR 1.10

I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" Service under 37 CFR 1.10 on the date indicated below and is addressed to Hon. Commissioner of Patents and Trademarks, Washington, DC 20231.

Signature Mary E. Bak

Date November 26, 1990

Exp. Mail #OB092 781293